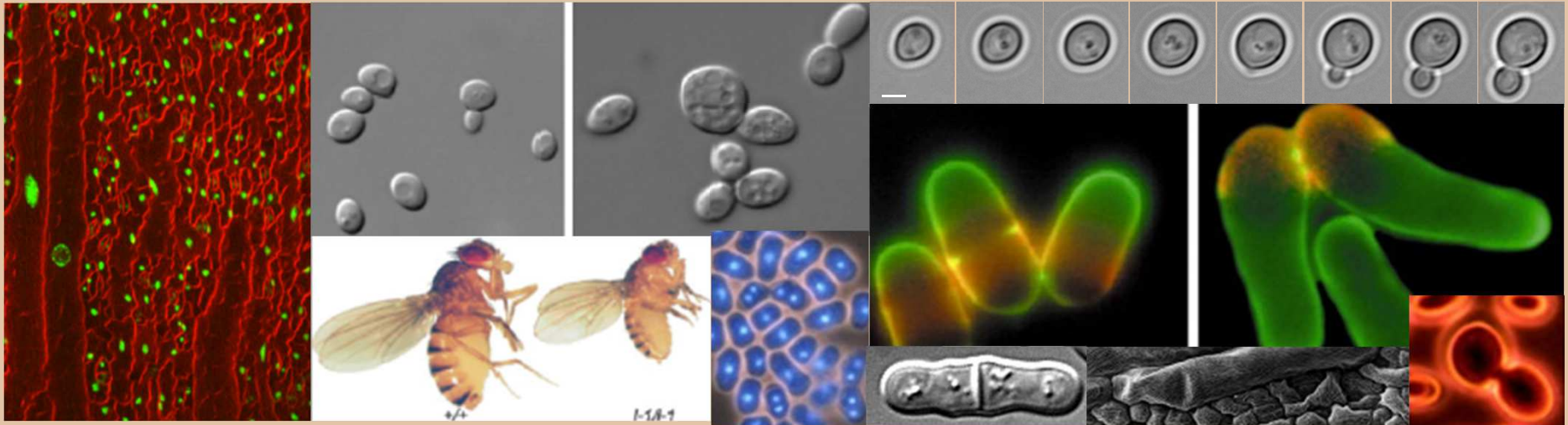


MODELS AND EXPERIMENTS TO UNDERSTAND CELL SIZE CONTROL



Attila Csikász-Nagy

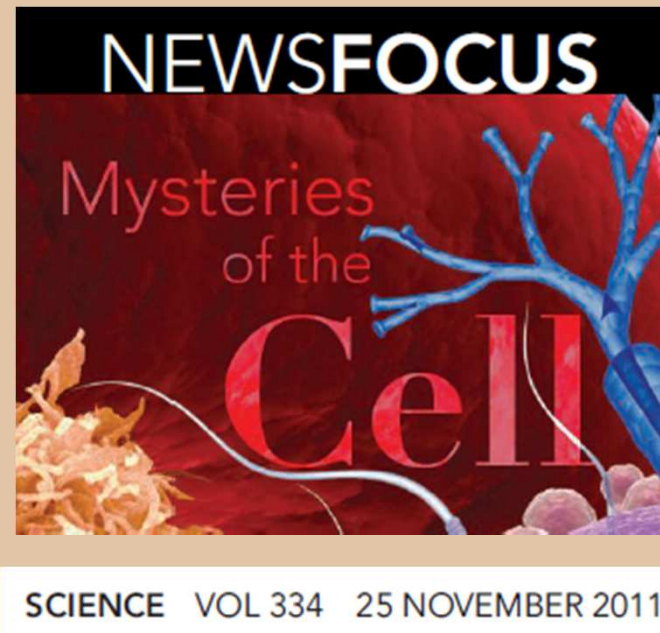
Randall Division of Cell and Molecular Biophysics
Institute for Mathematical and Molecular Biomedicine



Marti Aldea

IBMB, CSIS

How Does a Cell Know Its Size ?



What determines cell size?

Wallace F Marshall^{*1}, Kevin D Young², Matthew Swaffer³, Elizabeth Wood³, Paul Nurse^{3,4,5}, Akatsuki Kimura⁶, Joseph Frankel⁷, John Wallingford⁸, Virginia Walbot⁹, Xian Qu¹⁰ and Adrienne HK Roeder¹¹



Cell size in eukaryotes

Current Biology, Vol. 14, R1014–R1027 December 14, 2004,

How Cells Coordinate Growth and Division

Paul Jorgensen^{1,2} and Mike Tyers^{1,2}

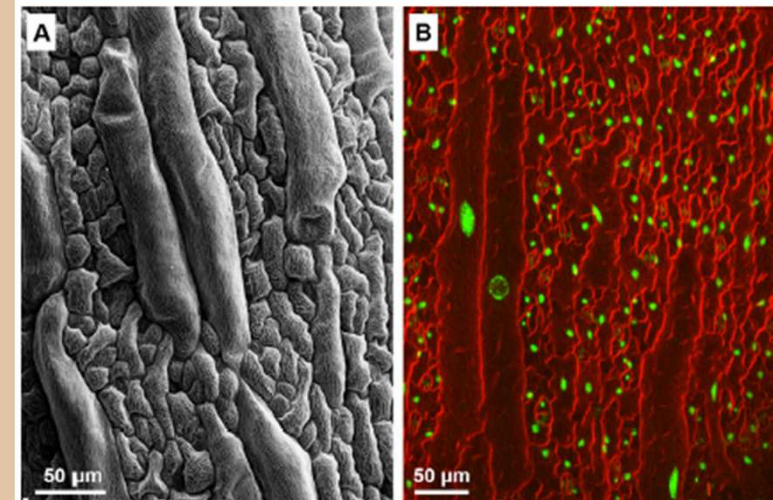
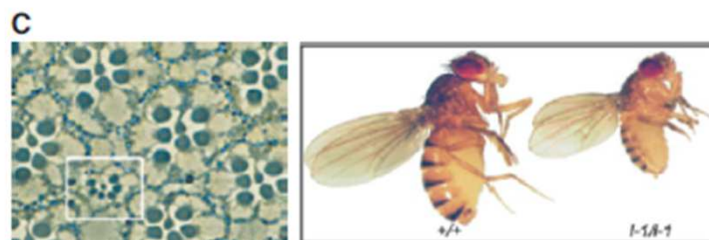
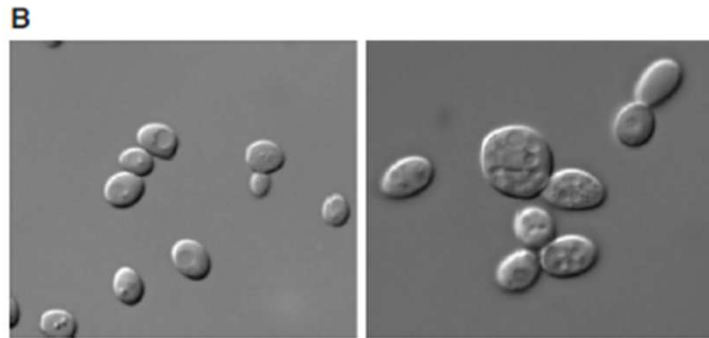
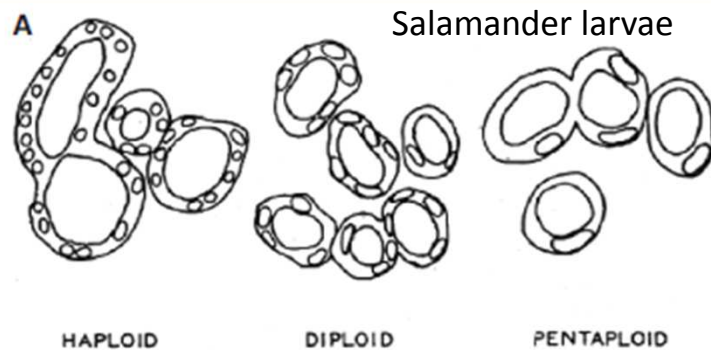
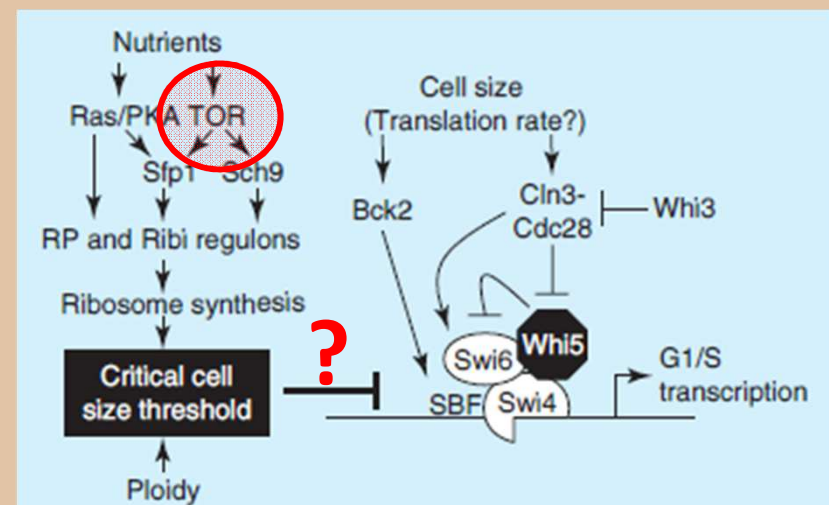


Figure 8. The diversity of cell sizes in the *Arabidopsis* sepal epidermis. (a) A scanning electron micrograph (SEM) of the sepal

What determines cell size? Marshall *et al.* *BMC Biology* 2012, 10:101

Wallace F Marshall^{1*}, Kevin D Young², Matthew Swaffer³, Elizabeth Wood³, Paul Nurse^{3,4,5}, Akatsuki Kimura⁶, Joseph Frankel⁷, John Wallingford⁸, Virginia Walbot⁹, Xian Qu¹⁰ and Adrienne HK Roeder¹¹



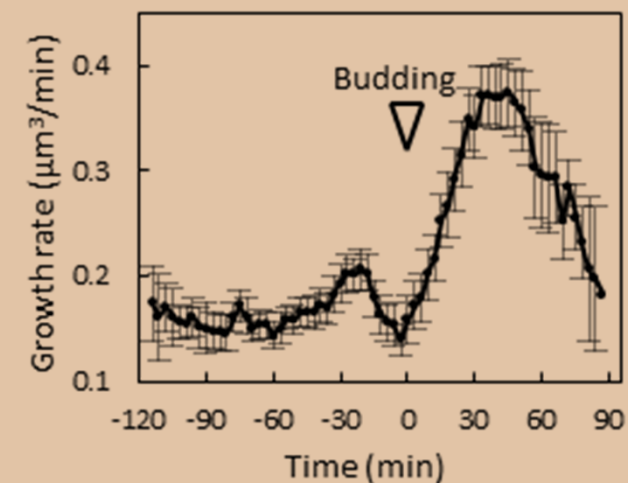
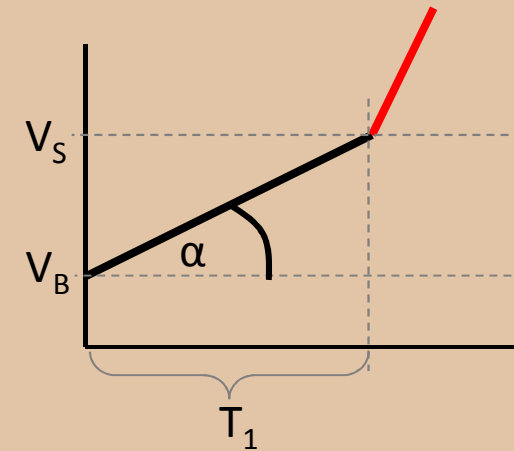
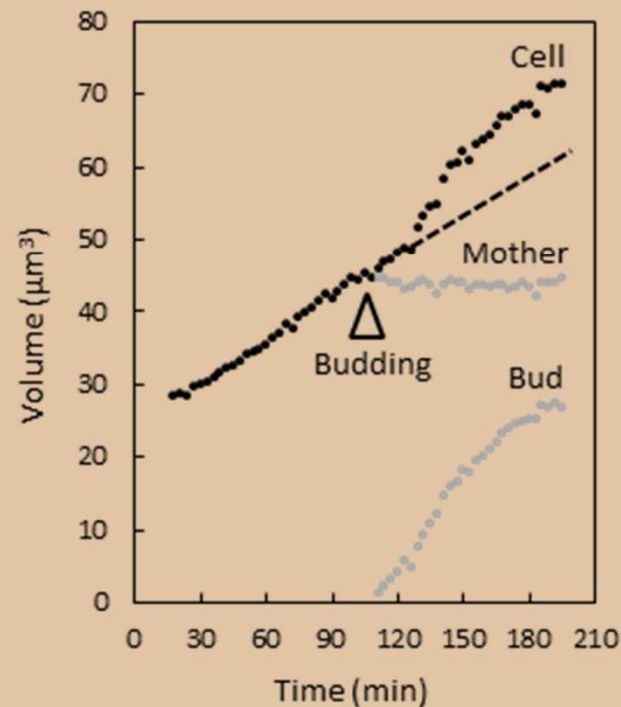
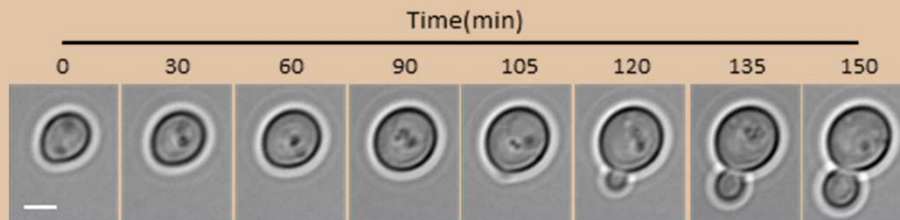
Size control in budding yeast

The critical size is set at a single-cell level by growth rate to attain homeostasis and adaptation

Francisco Ferrezuelo^{1,*}, Neus Colomina^{1,*}, Alida Palmisano^{2,3}, Eloi Gari¹, Carme Gallego⁴, Attila Csikász-Nagy² & Martí Aldea⁴



NATURE COMMUNICATIONS | 3:1012 | DOI: 10.1038/ncomms2015



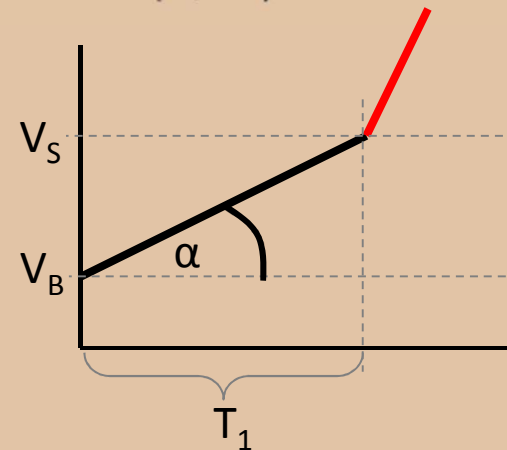
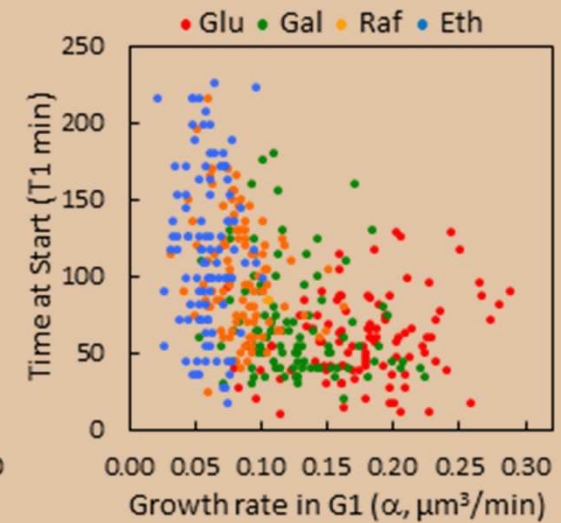
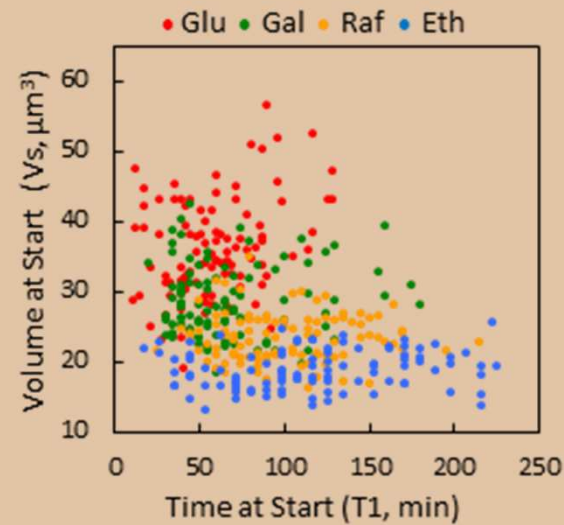
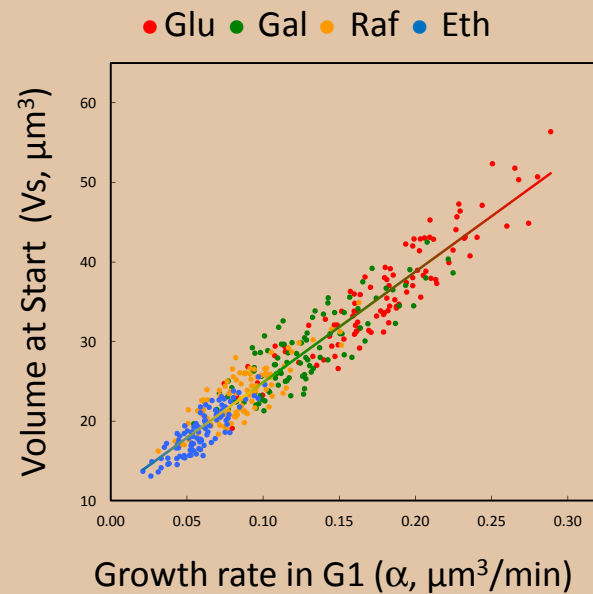
Critical size depends on growth rate

The critical size is set at a single-cell level by growth rate to attain homeostasis and adaptation

Francisco Ferrezuelo^{1,*}, Neus Colomina^{1,*}, Alida Palmisano^{2,3}, Eloi Gari¹, Carme Gallego⁴, Attila Csikász-Nagy² & Martí Aldea⁴



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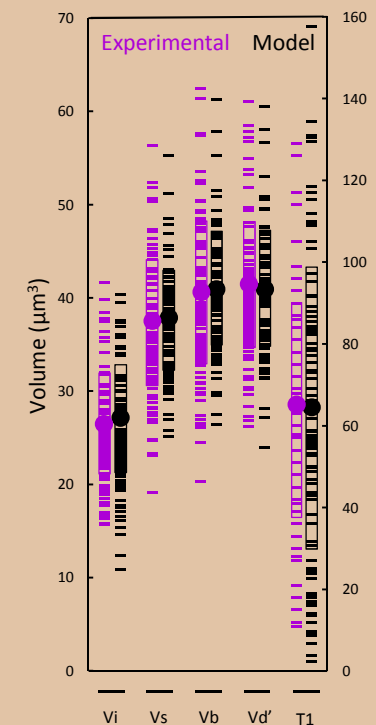
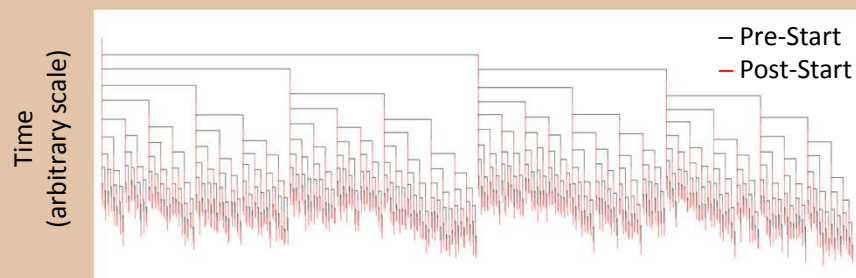
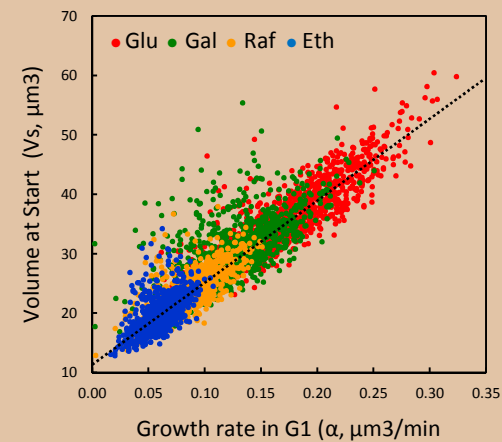
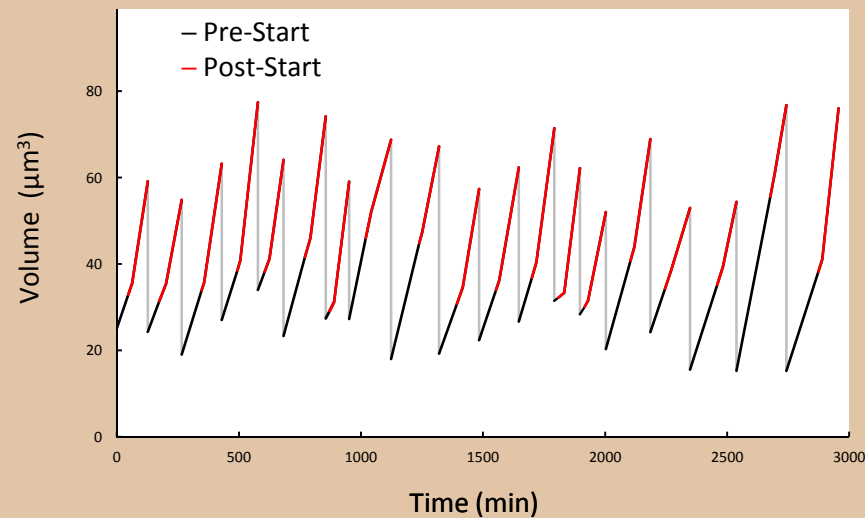
Computational model matches experimental results

The critical size is set at a single-cell level by growth rate to attain homeostasis and adaptation

Francisco Ferrezuelo^{1,*}, Neus Colomina^{1,*}, Alida Palmisano^{2,3}, Eloi Gari¹, Carme Gallego⁴, Attila Csikász-Nagy² & Martí Aldea⁴



NATURE COMMUNICATIONS | 3:1012 | DOI: 10.1038/ncomms2015



Computational model explains growth rate dependent size

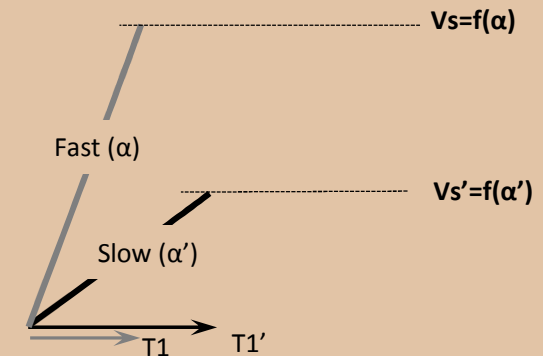
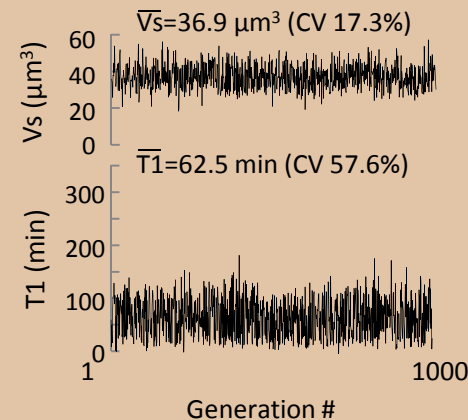
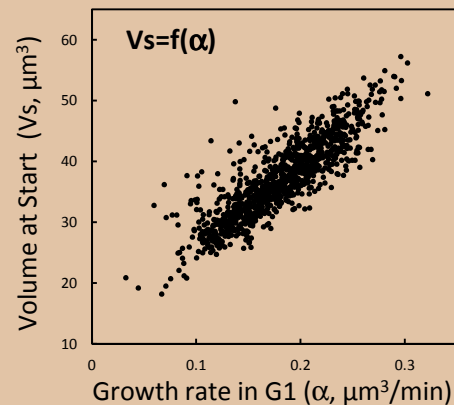
The critical size is set at a single-cell level by growth rate to attain homeostasis and adaptation

Francisco Ferrezuelo^{1,*}, Neus Colomina^{1,*}, Alida Palmisano^{2,3}, Eloi Gari¹, Carme Gallego⁴, Attila Csikász-Nagy² & Martí Aldea⁴

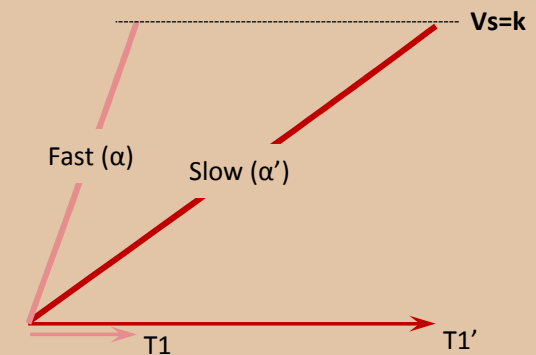
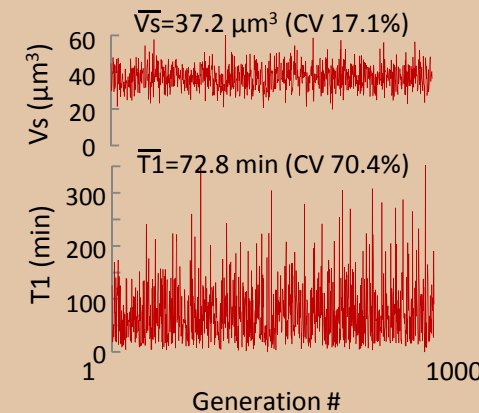
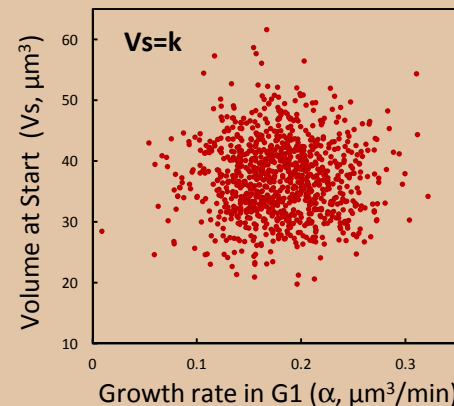


NATURE COMMUNICATIONS | 3:1012 | DOI: 10.1038/ncomms2015

**Growth rate
dependent
critical size**



**Fixed
critical size**



Size control perturbation in mutants

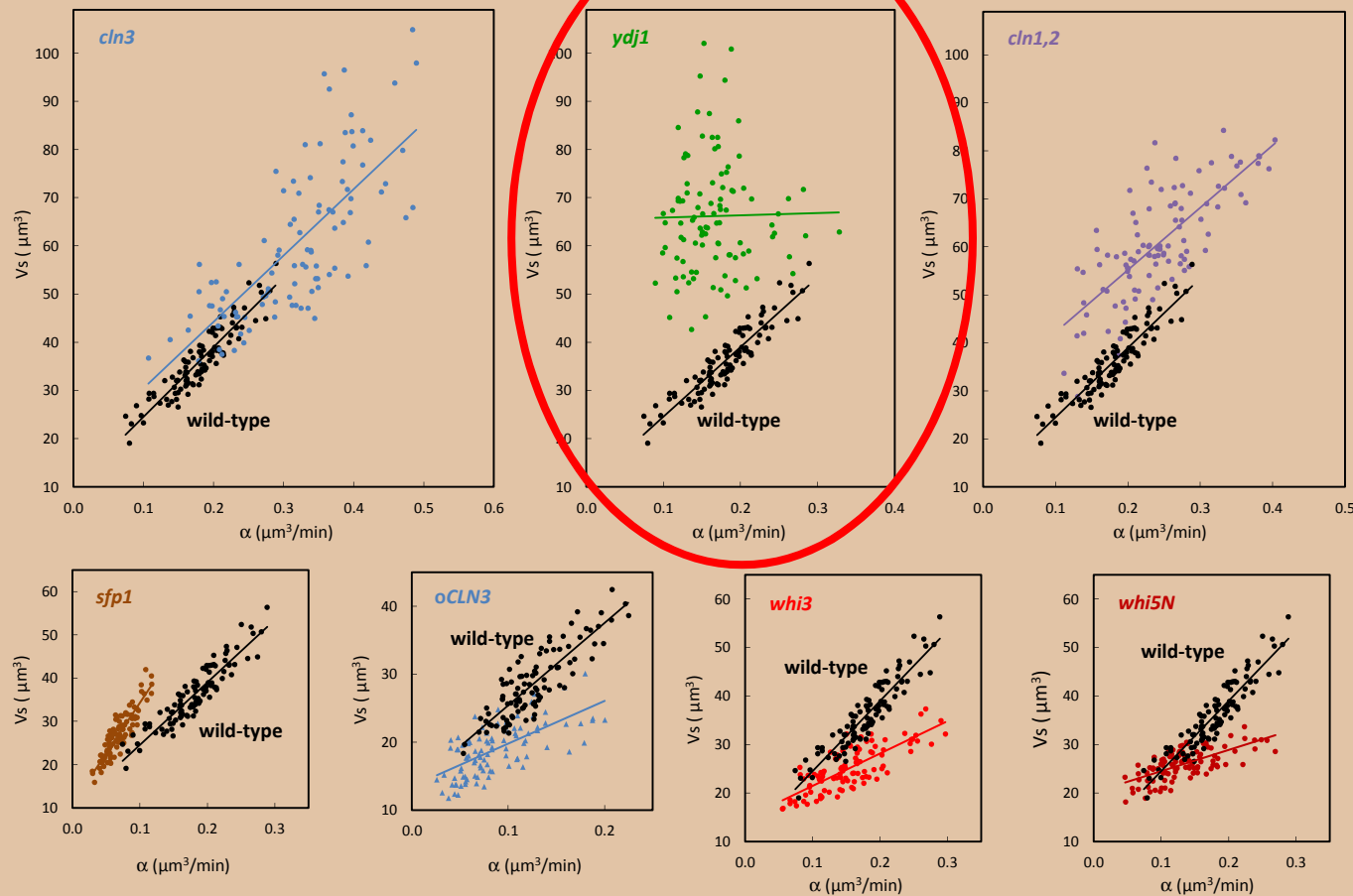
The critical size is set at a single-cell level by growth rate to attain homeostasis and adaptation

Francisco Ferrezuelo^{1,*}, Neus Colomina^{1,*}, Alida Palmisano^{2,3}, Eloi Gari¹, Carme Gallego⁴, Attila Csikász-Nagy² & Martí Aldea⁴



NATURE COMMUNICATIONS | 3:1612 | DOI: 10.1038/ncomms2015

Hsp40, DnaJ
chaperon



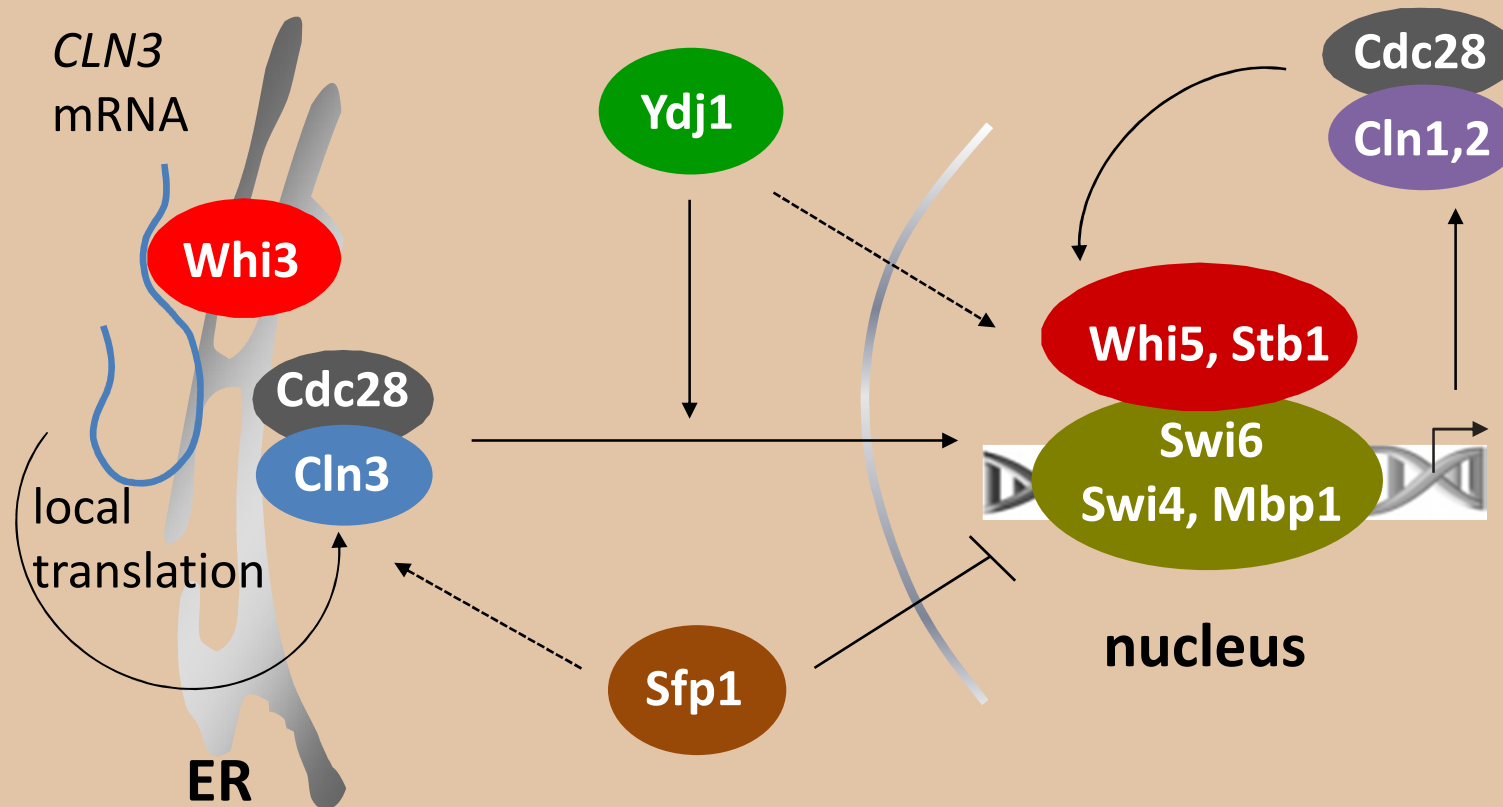
Chaperons connects growth to cell size?

The critical size is set at a single-cell level by growth rate to attain homeostasis and adaptation

Francisco Ferrezuelo^{1,*}, Neus Colomina^{1,*}, Alida Palmisano^{2,3}, Eloi Gari¹, Carme Gallego⁴, Attila Csikász-Nagy² & Martí Aldea⁴

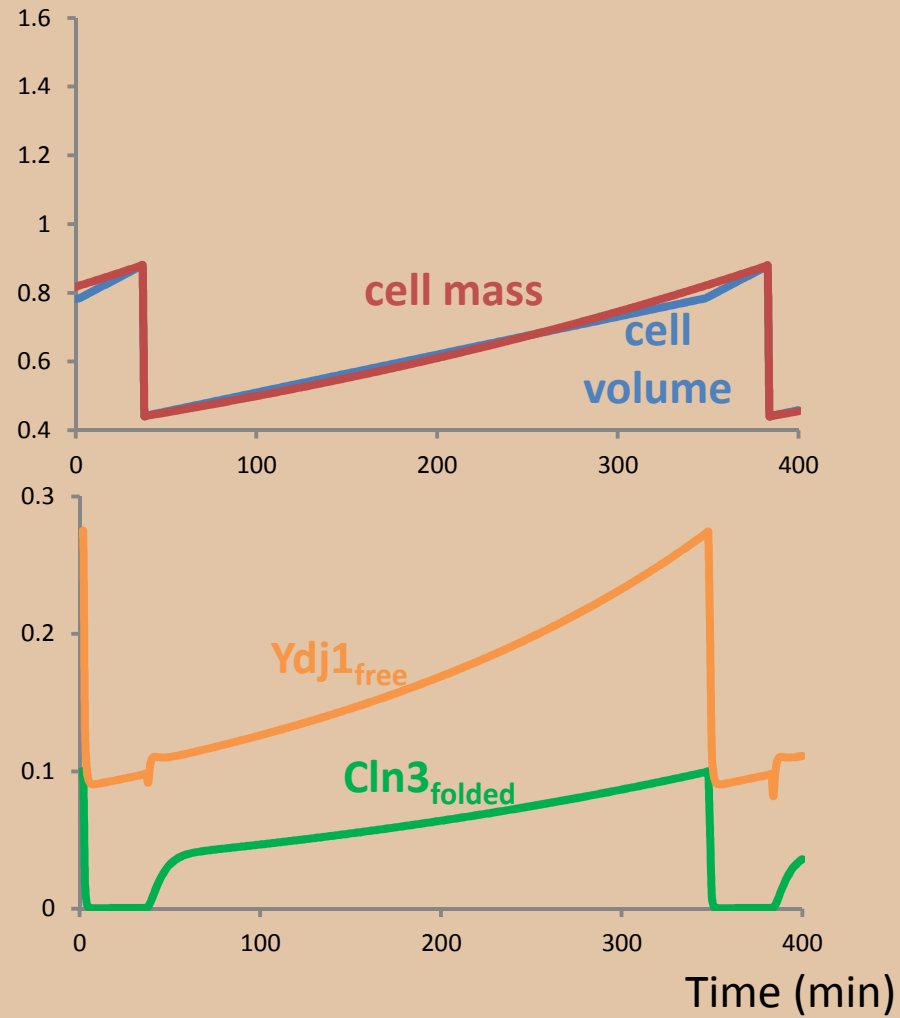


NATURE COMMUNICATIONS | 3:1012 | DOI: 10.1038/ncomms2015

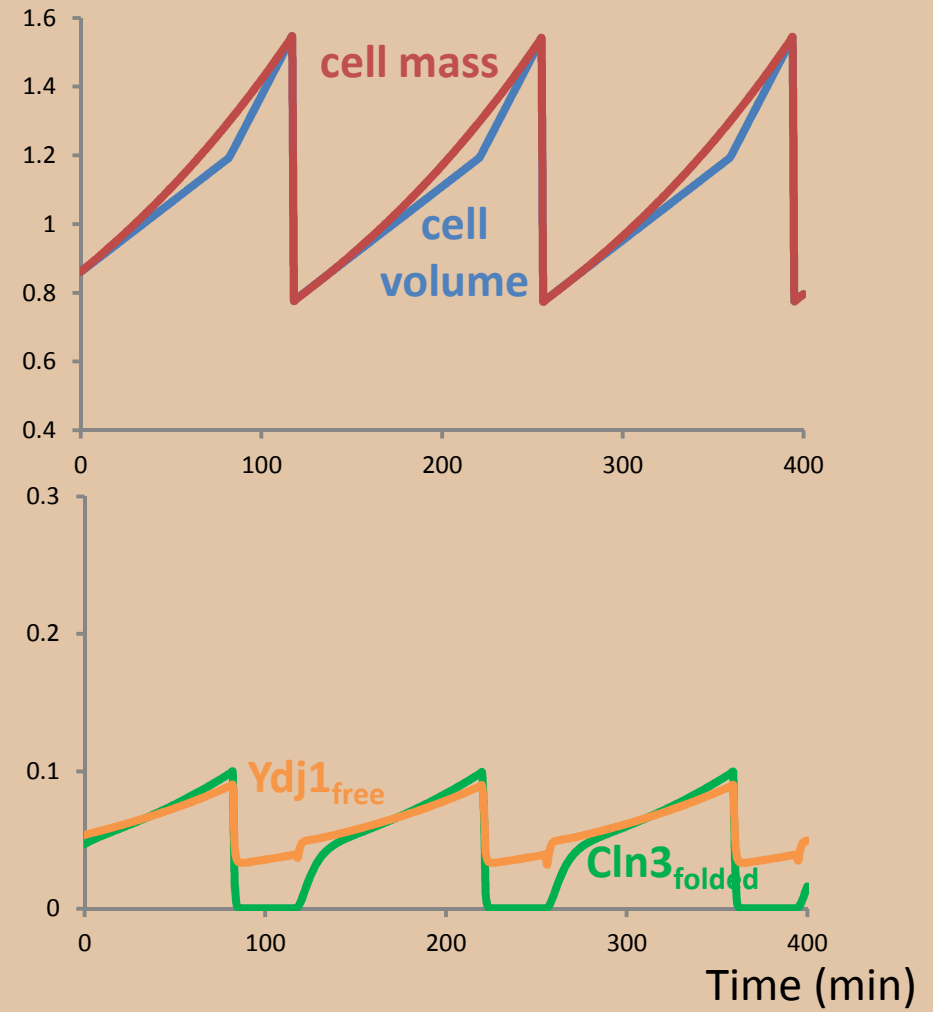


The 'speedometer' model

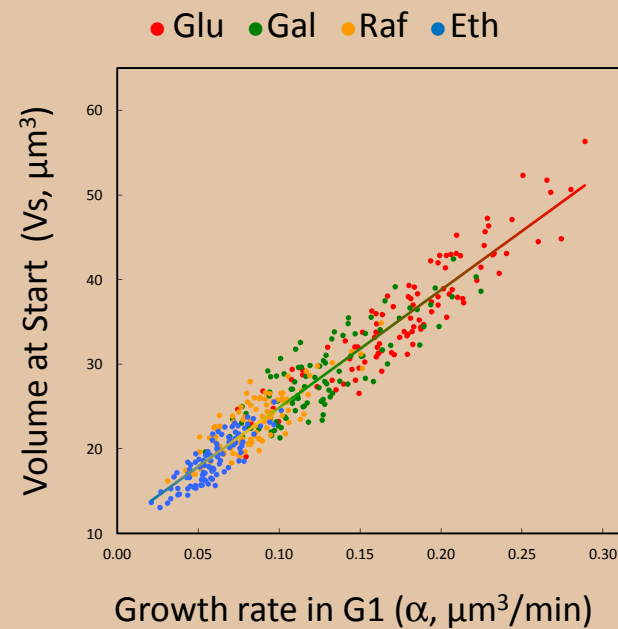
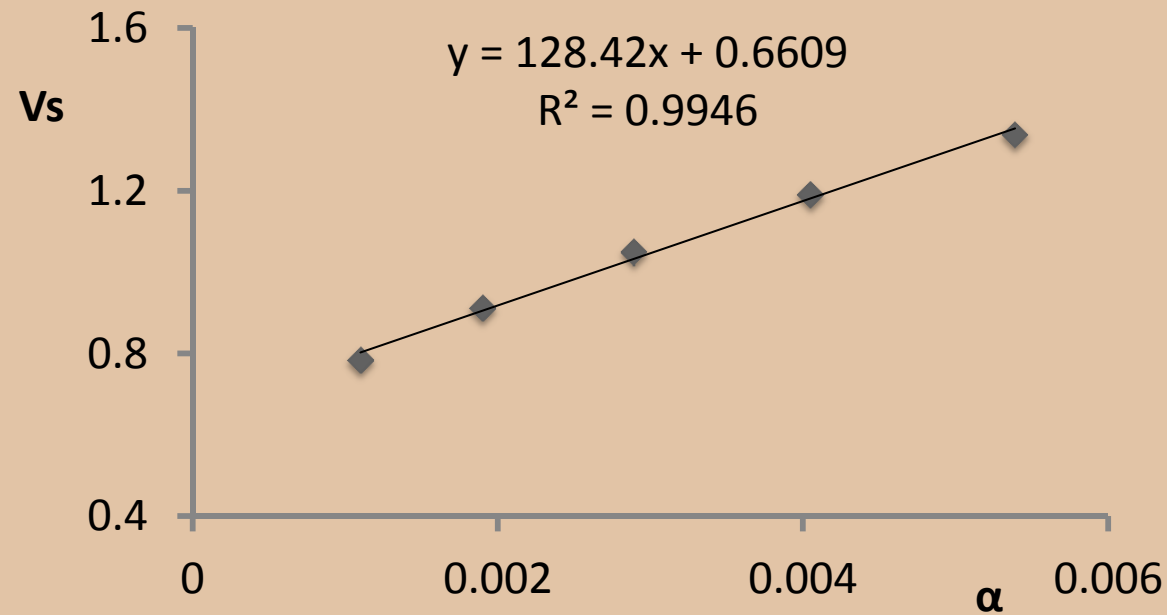
Mass doubling time: 350 min
 $\alpha = 0.0027$



Mass doubling time: 140 min
 $\alpha = 0.004$



The 'speedometer' model

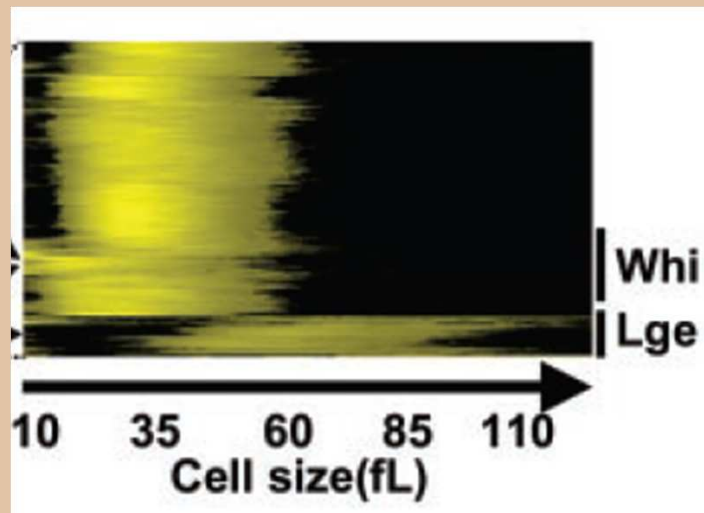


Finding the conserved cell size regulatory pathways

SCIENCE VOL 297 19 JULY 2002

Systematic Identification of Pathways That Couple Cell Growth and Division in Yeast

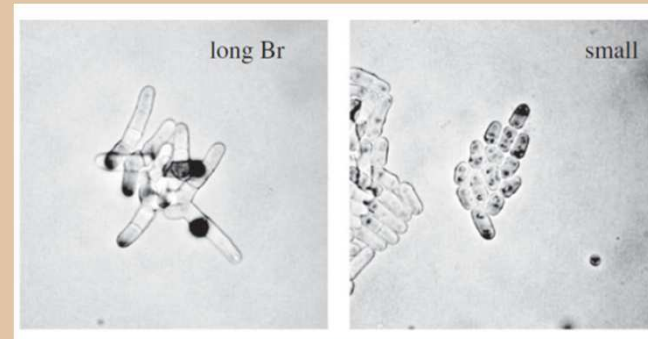
Paul Jorgensen,^{1,2*} Joy L. Nishikawa,^{1,2*} Bobby-Joe Breitkreutz,²
Mike Tyers^{1,2,†}



A genome-wide resource of cell cycle and cell shape genes of fission yeast

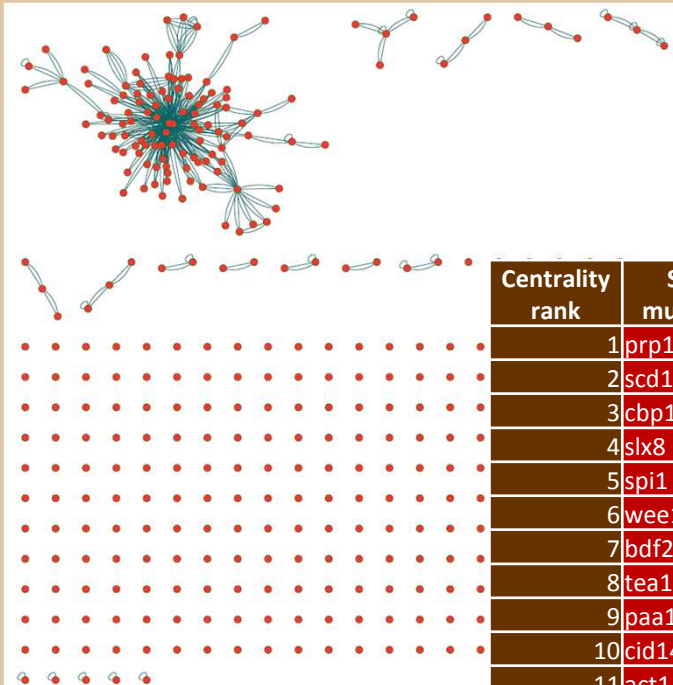
Jacqueline Hayles^{1,†}, Valerie Wood^{1,2,†}, Linda Jeffery^{1,†},
Kwang-Lae Hoe^{3,†}, Dong-Uk Kim^{4,†}, Han-Oh Park^{5,†},
Silvia Salas-Pino^{6,7}, Christian Heichinger^{6,8} and Paul Nurse^{1,6}

Open Biol 3: 130053



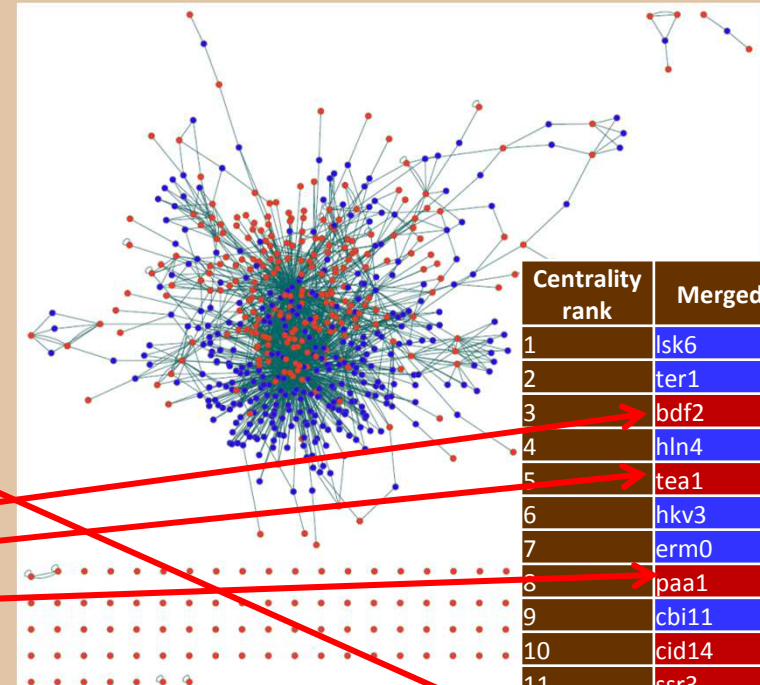
Building and analyzing a network of size regulators

S. pombe size mutants



Centrality rank	Size mutants
1	prp17
2	scd1
3	cbp1
4	slx8
5	spi1
6	wee1
7	bdf2
8	tea1
9	paa1
10	cid14
11	act1
12	rpb7
13	ssr3
14	cdc22
15	fib1
16	mto1
17	rpt5
18	adh1
19	cpc2
20	rpn11

S. pombe size mutants + first neighbours



Centrality rank	Merged
1	lsk6
2	ter1
3	bdf2
4	hln4
5	tea1
6	hkv3
7	erm0
8	paa1
9	cbi11
10	cid14
11	ssr3
12	skv3
13	lcf2
14	prp17
15	cdc22
16	act1
17	hsq13
18	rpb5
19	cmh6
20	rpt5

Linkers of Cell Polarity and Cell Cycle Regulation in the Fission Yeast Protein Interaction Network



Federico Vaggi¹, James Dodgson², Archana Bajpai¹, Anatole Chessel², Ferenc Jordán¹, Masamitsu Sato³, Rafael Edgardo Carazo-Salas², Attila Csikász-Nagy^{1*}

October 2012 | Volume 8 | Issue 10 | e1002732

Translating yeast data to other organisms

ORF IDs	Protein Names	Attribute	Systematic IDs	Protein Names	Attribute	Protein Names	TAIR ID
<i>S. cerevisiae</i>	<i>S. cerevisiae</i>	<i>S. cerevisiae</i>	<i>S. pombe</i>	<i>S. pombe</i>	<i>S. pombe</i>	<i>H. sapiens</i>	<i>A. thaliana</i>
YCR009C	RVG161	larger: Actin cytoskeleton	SPBC725.03c	hob3	long	PIN3	At4g27270
YDL082W	RPL13A	smaller: Ribosomal subunits	SPAC664.05	rpl13	germination	RPL13	At2g44950
YDL136W	RPL35B	smaller: Ribosomal subunits	SPCC613.05c	rpl35	spores	RPL35	At2g09990
YHR001W	QCR10	smaller: Mitochondrial function	SPBC1271.12	kes1	misshapen	OSBPL10	At5g57240
YHR158C	KEE1	smaller: Morphology function	SPCC1223.06	tea1	curved	RABEPK	At3g05420
YJL187C	SWE1	smaller: Cell cycle regulator	SPCC18B5.03	wee1	small	WEE2	At1g51850
YNL148C	ALF1	larger: Cell cycle regulator	SPAC13D5.05	alp11	curved	TBCB	At3g10220
YOL004W	SIN3	larger: RNA Pol II complex	SPBC17C2.10c	pst1	long	SIN3A	At5g10960
YPL031C	PHO85	smaller: DNG Glicerol	SPCC16C4.11	pef1	misshapen	CDK5	At5g39840
YPR135W	POB1	larger: Cell cycle regulator	SPAPB1E7.02c	mcl1	long	WDHD1	At1g42660
...

Marti Aldea



Rafael Carazo-Salas



Shaun N. Thomas



Azeddine SiAmmour

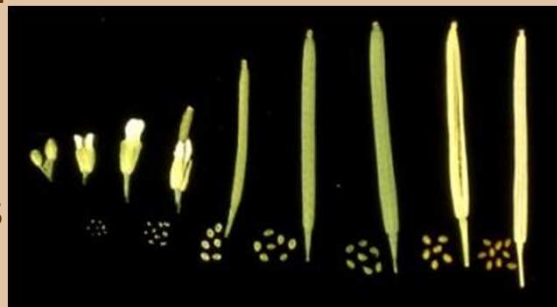


Size control in *Arabidopsis* and apple



Measuring at various time points:

- Size of leaves
- Size of floral ramp
- Root length
- Root diameter
- Size of silique
- Number of seeds
- Size of seeds



Checking the expression of candidate genes in different size apple varieties to identify control on fruit size.

Acknowledgements



Shaun B. Thomas



Zoltán Dúl



Rafael Carazo-Salas



Valentina Cappelletti



Federico Vaggi



Azeddine SiAmmour



Duccio Cavalieri

Aldea group



Thank you!